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Scientific Article

A Potential Pitfall and Clinical Solutions in Surface-Guided Deep Inspiration Breath Hold Radiation Therapy for Left-Sided Breast Cancer

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Purpose: Deep inspiration breath hold (DIBH) is an effective technique to spare the heart in treating left-sided breast cancer. Surface-guided radiation therapy (SGRT) is increasingly applied in DIBH setup and motion monitoring. Patient-specific breathing behavior, either thoracically driven or abdominally driven (A-DIBH), should be unaltered, online identified, and monitored accordingly to ensure reproducible heart-sparing treatment.

Methods and Materials: Sixty patients with left-sided breast cancer treated with SGRT were analyzed: 20 A-DIBH patients with vertical chest elevation (VCE $\leq$ 5 mm) were prospectively identified, and 40 control patients were retrospectively and randomly selected for comparison. At simulation, both free-breathing (FB) and DIBH computed tomography (CT) were acquired, guided by a motion surrogate placed around the xiphoid process. For SGRT treatment setups, the region of interest (ROI) was defined on the CT chest surface, and the surrogate-based setup was a backup. For all 60 patients, the VCE was measured as the average of the FB-to-DIBH elevations at the breast and xiphoid process, together with abdominal elevation. In the 40-patient control group, A-DIBH patients (VCE $\leq$ 5 mm) were identified. Of the 20 A-DIBH patients, 10 were treated with volumetric modulated arc therapy plans, and 10 patients were treated with tangent plans. Clinical DIBH plans were recalculated on FB CT to compare maximum dose (D_{Max}), 5% of the maximum dose ($D_{5\%}$), mean dose (D_{Mean}), and V_{30Gy}, V_{20Gy}, and V_{5Gy} of the heart and lungs and their significance.

Results: In the 20 A-DIBH patients, VCE = 3 ± 2 mm, surrogate motion (9 ± 6 mm), and abdomen motion of 14 ± 5 mm are found. Heart dose reduction from FB to DIBH is significant ($P < .01$): $\Delta D_{Max} = -8.4 \pm 9.8$ Gy, $\Delta D_{5\%} = -2.4 \pm 4.4$ Gy, and $\Delta D_{Mean} = -0.6 \pm 0.9$ Gy. Six out of 40 control patients (15%) are found to have VCE $\leq$ 5 mm.

Conclusions: A-DIBH (VCE $\leq$ 5 mm) patient population is significant (15%), and they should be identified in the SGRT workflow and monitored accordingly. A new abdominal ROI or an abdominal surrogate should be used instead of the conventional chest-only ROI. Patient-specific DIBH should be preserved for higher reproducibility to ensure heart sparing.

Introduction

Deep inspiration breath hold (DIBH) has been used for radiation therapy of patients with left-sided breast cancer for about 2 decades to spare the heart as vertical chest wall elevation (VCE) at DIBH separates the heart from

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the chest wall in the supine position due to gravity and/or inferior shift due to diaphragmatic pull. Clinical data have shown that DIBH is very effective in reducing heart toxicity from breast irradiation,[1,2] even for some patients who may not reproduce DIBH completely at treatment.[2,3] Alternatively, the prone treatment can be used to spare the heart and lungs, but it is difficult to cover local lymph nodes, so it may not be suitable for treating patients with nodal involvement.[2] Initially, a surrogate-guided technique was developed using a surrogate box placed near the xiphoid process to monitor the chest elevation, such as a real-time positioning management (RPM, Varian Medical Systems, Palo Alto, CA) system or its newer version, respiratory gating for scanners (RGSC). However, the variation of RPM or RGSC box placement throughout a multifractional radiation therapy treatment course introduces uncertainty in monitoring DIBH levels. To eliminate the surrogate placement uncertainty, surface-guided radiation therapy (SGRT) has been developed and implemented in the clinic for left-breast DIBH treatment.[4-6] Although the region of interest (ROI) defined for breast SGRT setup and motion monitoring may vary, the chest wall surface has been used to achieve DIBH for treatment.[7,8] A popular ROI includes the breast and surrounding area with a unique landscape,[8,9] namely a chest-only ROI. Furthermore, the SGRT technique allows aligning of the ipsilateral arm and chin first at free-breathing (FB) before DIBH, minimizing the breast deformation for partial breast irradiation and reproducing the position of the axillary and supraclavicular lymph nodes for patients with locally advanced breast cancer.[8,10] Moreover, recent advances in SGRT have promised to remove the need for tattoos in conventional patient setups using room lasers for patient alignment, including left-sided DIBH breast treatment.[11-13] Therefore, the SGRT technique has been increasingly applied in DIBH radiation therapy for left-sided breast cancer.

To ensure a reproducible DIBH, offline patient training can be applied, facilitating DIBH simulation and treatment for better compliance and reproducibility,[9,14] and online visual coaching seems necessary so that patients can consistently control the extent of DIBH with guidance.[4,15] Thoracic-driven DIBH (T-DIBH) and abdominal-driven DIBH (A-DIBH) have been recently studied and brought to the attention of clinicians that both offer heart sparing.[16-18] Because the training/coaching approach will alter some patients' native breathing behavior, training must be reinforced, and patients' participation via visual coaching is required to ensure consistent T-DIBH or A-DIBH from simulation to the entire multifractional treatment. Although this is a widely studied and adopted method, it has its shortcomings, including higher clinical workload and the likelihood of breathing pattern changes,[15] namely falling back to the natural behavior. In addition, changing patients' native breathing behavior may be a challenge for some patients, as a recent study showed that 20 of 120 patients (17%) cannot distinguish between T-DIBH and A-DIBH at simulation,[18] so training such patients may not be feasible. Furthermore, when an ROI is drawn on the chest surface only as the default ROI, it implies that the patients are going through T-DIBH predominantly using the intercoastal muscles with sufficient chest elevation. This default ROI may not apply to monitor A-DIBH as it does not cover the abdominal surface.

Alternatively, the actual patient-specific breathing behavior can be preserved in the DIBH treatment by identifying a patient as thoracic-breathing or abdominal-breathing early in the clinical workflow (the simulation-planning-treatment process) using the VCE measure, as well as providing a simple, adaptive DIBH monitoring strategy to T-DIBH or A-DIBH patients. As a patient's natural breathing behavior is more reproducible, it would lead to a more consistent treatment outcome with potentially less demand for daily maintenance. This rationale forms the hypothesis of the study to pursue and test, aiming at a feasible alternative clinical approach.

In this study, we prospectively identified 20 patients with left-sided breast cancer with A-DIBH, namely VCE $\leq$ 5 mm between FB and DIBH surfaces, measured the heart separation from the chest wall, compared the difference between FB and DIBH, and provided feasible solutions to monitor patients with A-DIBH properly using an abdominal ROI or the RPM/RGSC inferior to the xiphoid process. To demonstrate the worst-case-scenario dosimetric consequence for incorrect A-DIBH motion monitoring, the clinical DIBH plans were recalculated on FB computed tomography (CT) for comparison. Finally, to assess the scale of this clinical issue, we retrospectively and randomly selected 40 DIBH patients with left-breast cancer and quantified the percentage of abdominal-breathing patients (VCE $\leq$ 5 mm with A-DIBH), illustrating the potential clinical effect .

Methods and Materials

Selection of A-DIBH and control DIBH patients from SGRT treatments

In this study, we identified 20 DIBH patients with left-sided breast cancer with A-DIBH or VCE $\leq$ 5 mm between FB and DIBH CT surfaces prospectively in the clinical planning and plan checking process, raising the concern about the inability of the chest-only ROI to distinguish such patients' DIBH from FB owing to limited VCE. Clinically, planners and plan checkers were called upon to report any patients with breast cancer for DIBH SGRT with VCE $\leq$ 5 mm and changed the DIBH monitoring method from AlignRT (v6.2/v6.3, VisionRT, London, UK) to RPM/RGSC (Varian Medical Systems, Palo

Alto, CA). Among the 20 eligible patients, 10 were treated with volumetric modulated arc therapy (VMAT) for locally advanced breast cancer, and the other 10 were treated with opposite tangent fields. Nine of the 10 tangent plans were 2 fields treating early stage cancer, and 1 was 4 fields (opposite tangents plus supraclavicular field and posterior axillary boost field) treating locally advanced disease. These patients were analyzed both anatomically and dosimetrically to provide clinically feasible solutions.

To assess the scope of the clinical issue of A-DIBH, another 40 patients with left-sided breast cancer were randomly selected from our AlignRT-guided DIBH database as a control patient group. The body surface elevations at the chest and abdomen were measured to identify the A-DIBH patients, compare the difference in heart position at the anterior and lateral edges between FB and DIBH, and assess the distribution of VCE among the patients. The motion of the surrogate placed near the xiphoid process was assessed by locating the optical reflectors on the surrogate box (n = 2 for RPM and n = 4 for RGSC), measuring their vertical motions, and averaging them to represent the surrogate motion. The difference between the SGRT and surrogate-guided DIBH-monitoring techniques was analyzed.

Measurements of external surface elevation based on FB and DIBH simulation CTs

For each of the 60 DIBH patients, 3 sets of external surface elevation were measured based on the differences between FB and DIBH simulation CT scans at the center of the breast, the xiphoid process, and the abdomen (the maximal elevation point inferior to the xiphoid process), as shown in Fig. 1. The average of the first 2 measurements (at the breast and xiphoid process) was used to estimate the VCE value within the ROI, which should be above the average ROI motion as the upper chest usually moved less. The maximal abdominal elevation was measured on the CT image sets, usually near the inferior border of the field of view (FOV), which was about 10 to 20 cm inferior to the xiphoid process.

Additionally, the surrogate motion (RPM or RGSC), their placement location, and the default gating upper and lower thresholds were measured. The vertical motion of the RPM or RGSC box (Fig. 1B, C) was the average of all reflectors on the surrogate (2 for RPM and 4 for RGSC), and the default gating thresholds were determined from the breathing curve at simulation and recorded in the ARIA system (Varian Medical Systems, Palo Alto, CA). This motion may or may not be sufficient depending on the placement location. For all 60 patients, the VCE at the chest ROI, the surrogate motion, and the maximal abdominal elevation inferior to the xiphoid process were measured. The abdominal elevation was examined to determine whether a better box placement location existed with a larger vertical motion, especially for patients with limited VCE, or how much the abdominal surface should be covered by a second alternative ROI for A-DIBH motion monitoring (see Fig. 1).

Plan dosimetric evaluation of heart and lung sparing from FB to DIBH

When treating A-DIBH patients with VCE ≤ 5 mm, SGRT would fail to distinguish whether a patient was in DIBH or FB due to the clinical tolerance of ±3 mm/±3° configured for the AlignRT system in 6° of freedom. In the worst-case scenario, the patient may be treated in FB status completely as opposed to planned DIBH status, resulting in little gain in sparing the organs at risk (OARs), such as the heart and lungs. To quantify the dosimetric effect, we compared the doses to the heart and the lungs between the

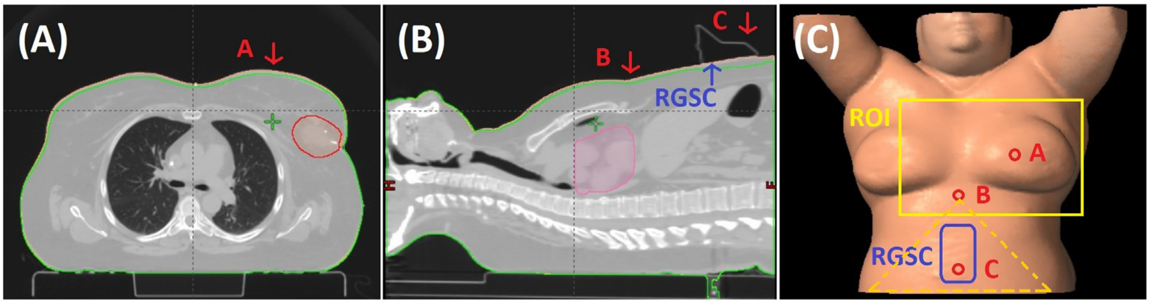

Figure 1 Illustration of measurement of vertical body surface elevation at (A) the breast, (B) the xiphoid process, and (C) the abdomen. The default chest-only ROI (solid yellow rectangle) for surface-guided radiation therapy setup in free-breathing and thoracic-driven deep inspiration breath hold (DIBH) motion monitoring, and an alternative abdomen ROI (dotted yellow triangle) for abdominal-driven DIBH motion monitoring are shown. The vertical chest elevation of the ROI is estimated as the average of those at points A and B. The respiratory gating for scanners (length = 7.4 cm) is visible in the DIBH computed tomography (light gray) with superimposed free-breathing body contour (green). *Abbreviations:* DIBH = deep inspiration breath hold; ROI = region of interest.

clinical DIBH plan and recalculated the FB plan with the same beams from the DIBH plan, simulating the aforementioned worst clinical scenario. Several dosimetric parameters were evaluated for the heart (mean dose [D_{Mean}], maximum dose [D_{Max}], 5% of the maximum dose [$D_{5\%}$], $V_{20\ Gy}$, $V_{30\ Gy}$) and both lungs ($V_{20\ Gy}$, $V_{10\ Gy}$, $V_{5\ Gy}$, D_{Mean}). These doses were compared between the DIBH and FB plans to quantify OAR sparing among the abdominal-breathing patients, the statistical significance, and explanation of the sparing effects based on the shape and location of the OARs, most importantly the heart.

Results

Different anterior body elevations from FB to DIBH for A-DIBH breast patients

For abdominal-breathing patients, the heart position shift (inferiorly) and shape change (elongated) owing to the pull from the diaphragm in A-DIBH provides the mechanism for heart sparing in both VMAT and tangent planning, as shown in Fig. 2. Although the external VCE is small, the heart position and shape changes from FB to A-DIBH occur in the abdominal-breathing patients at various extents, allowing for heart sparing when DIBH is achieved.

Table 1 tabulates all 20 patients with left-sided breast cancer with little VCE at A-DIBH. The first 10 patients with the locally advanced disease are treated with VMAT, whereas the other 10 patients are mostly at the early stage and treated with tangent plans. The vertical elevations at the chest surface and abdominal surface are listed, together with the motion of the surrogate (RPM or RGSC) that is visible in the simulation FB and DIBH CT images. Although the VCE (averaged at the breast and xiphoid process) is very small (3 ± 2 mm), the motion of the surrogate is large enough (10 ± 6 mm) near the xiphoid process due to the finite sizes of the surrogates (RPM: 34 mm and RGSC: 74 mm along the superior-inferior direction). The elevation at the abdomen (15 ± 6

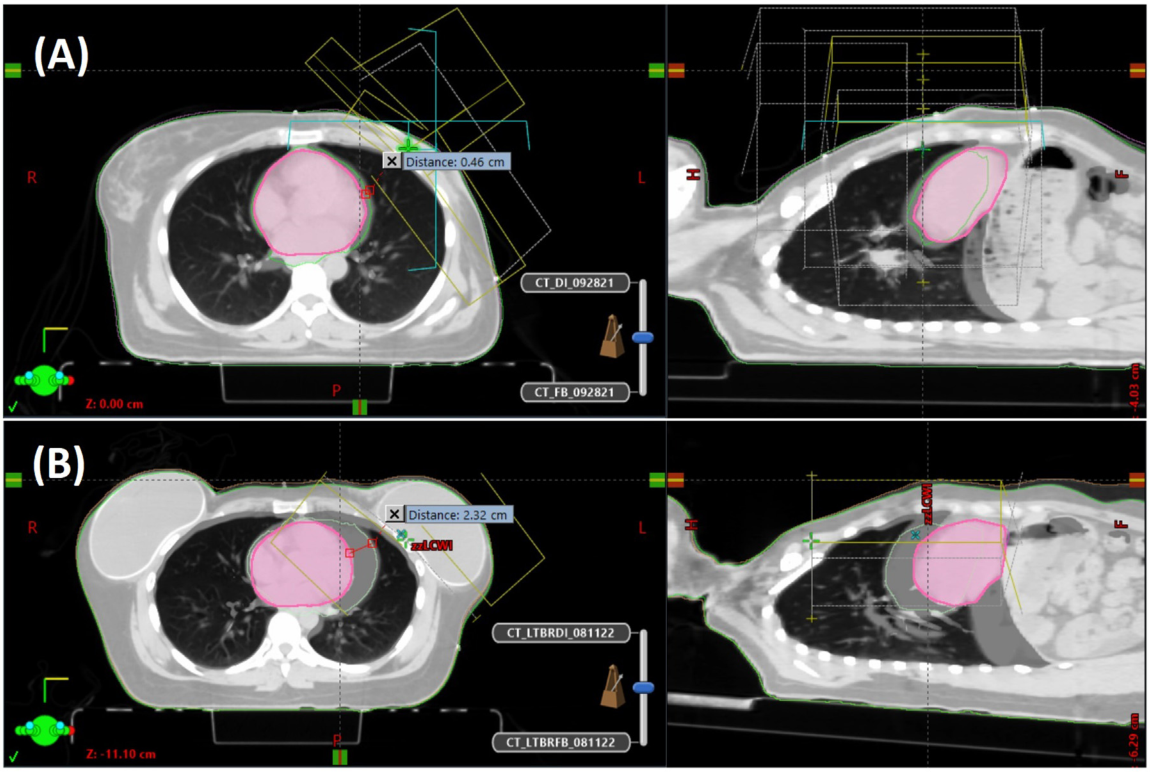

Figure 2 Two examples of heart elongation and position change for abdominal-driven deep inspiration breath hold (DIBH) in patients with little vertical chest wall elevation (VCE). (A) Patient #1 (mastectomy; VCE = 1 mm; volumetric arc therapy; heart maximum dose reduction of 4.6 Gy) on a flat breast board, and (B) patient #16 (implant; VCE = 4 mm; tangents; heart maximum dose reduction of 27.8 Gy) on a tilted board. Both axial and sagittal views are shown. The heart contour is pink in DIBH and green in free-breathing. Body contour is brown in DIBH and green in free-breathing. The green cross mark on the left chest wall is the treatment isocenter. *Abbreviations:* DIBH = deep inspiration breath hold; VCE = vertical chest wall elevation.

Table 1 Anterior body surface elevation and surrogate motion for 20 patients with left-sided breast cancer with abdominal-driven deep inspiration breath hold and little vertical chest elevation

				Chest surface elevation (mm)		Surrogate motion (mm)			Abdomen surface elevation (mm)	
Patient	Age	Breast status	Plan tech	Breast*	Xiphoid	Device	Motion	Location†	Motion	Location†
1	44	M	V	0.0	1.6	RPM	5.0	61.6	7.5	136.5
2	61	L	V	0.4	2.7	-	-	-	14.1	76.1
3	47	M	V	−0.6	4.1	RPM	25.0	96.7	28.1	129.6
4	47	I	V	5.3	4.9	RGSC	13.0	59.4	18.2	135.9
5	86	M	V	4.9	3.6	RPM	19.7	117.2	20.0	100.0
6	52	I	V	0.8	1.1	RPM	1.3	108.4	13.0	129.5
7	75	L	V	3.9	5.7	RPM	5.3	61.8	11.1	111.1
8	57	M	V	5.4	4.9	RPM	9.3	24.0	7.7	77.2
9	34	M	V	4.5	5.3	RGSC	5.2	99.0	11.1	111.2
10	40	I	V	5.0	5.3	RPM	14.8	123.1	9.9	99.2
11	46	L	T	1.0	3.7	RGSC	12.5	117.3	13.0	128.2
12	74	L	T	1.6	0.6	RGSC	8.0	120.1	20.7	142.7
13	75	L	T	2.1	4.3	RPM	4.0	138.3	9.7	94.8
14	65	L	T	−2.5	−3.5	RGSC	4.7	86.5	11.7	142.7
15	59	L	T	5.2	4.3	RGSC	7.3	77.3	15.1	104.4
16	37	I	T	3.1	5.9	RPM	10.6	62.6	21.5	156.3
17	34	L	T	3.7	3.3	RPM	3.5	58.1	12.4	110.9
18	65	L	T	3.6	2.8	RGSC	3.6	81.3	12.2	133.6
19	61	L	T	4.3	4.5	RGSC	10.2	163.4	12.4	141.9
20	65	L	T	3.7	2.9	RGSC	6.1	83.2	10.3	99.3
AVG	56	-	-	2.8	3.4	-	8.9	91.5	14.0	118.1
STD	15	-	-	2.3	2.2	-	6.0	33.8	5.2	22.8

Abbreviations: AVG = average; I = implant; L = lumpectomy; M = mastectomy; RGSC = respiratory gating for scanners with the box longitudinal length of 74 mm; RPM = real-time positioning management with the box longitudinal length of 34 mm; STD = standard deviation; T = tangents; V = volumetric arc therapy; VCE = mean vertical chest elevation between the breast isocenter and the xiphoid process. Plan Tech = planning technique.

* The isocenter within the left breast is used to measure the vertical elevation.

† The locations are from the xiphoid process to either the inferior end of the surrogate box or the abdominal point where the elevation is the largest.

mm) is even larger and more sensitive in monitoring A-DIBH.

Plan dosimetry comparison between FB and DIBH for heart and lung sparing

The DIBH plans and FB plans for the 20 patients are compared in pairs regarding heart dose. The dose reduction from FB to DIBH is significant ($P < .05$) in $\Delta D_{Max} = -8.4 \pm 9.8$ Gy, $\Delta D_{5\%} = -2.4 \pm 4.4$ Gy, and $\Delta D_{Mean} = -0.6 \pm 0.9$ Gy. Although the dose reduction in the ipsilateral lung is also observed, it is trivial and not clinically significant (<1% on average). For the 10 VMAT plans, heart dose-sparing results from FB to DIBH are shown in Table 2, and for the 10 tangent plans, heart dose sparing is even more pronounced ($\Delta D_{Max} = -11.6 \pm 10.8$ Gy; $P = .008$) in Table 3. This is because the dose falloff from in-field to out-of-field in tangent plans is sharper than in VMAT plans. The 10 VMAT patients and a 4-field patient (#16) have locally advanced breast cancer (most with mastectomy or implant) and are treated with breast and regional nodal irradiation. The remaining 9 tangent (2F) patients have early stage breast cancer with lumpectomy. There is 1 VMAT case and 1 tangent case with the heart dose slightly higher in A-DIBH than in FB, but both are below the average heart dose in their VMAT or tangent groups, respectively.

It is worthwhile to note that VMAT plans have relatively higher heart doses (D_{Max}, $D_{5\%}$, and D_{Mean}) than the tangent plans because multiple beam angles are applied, and some exit through the heart, leading

Table 2 Heart dose sparing based on VMAT plan dosimetry comparison between FB and DIBH for patients with left-sided breast cancer with abdominal-driven breathing and little vertical chest elevation ($\leq$5 mm)

	Planning		FB (heart, cGy)			DIBH (heart, cGy)			Heart sparing (cGy)		
Patient	Plan	Rx (cGy)	D_{Mean}	D_{Max}	$D_{5\%}$	D_{Mean}	D_{Max}	$D_{5\%}$	D_{Mean}	D_{Max}	$D_{5\%}$
1	VMAT	200 × 25	379	2326	954	370	1871	958	−10	−455	4
2	VMAT	200 × 25	626	4180	1687	489	3378	1096	−137	−802	−591
3	VMAT	200 × 25	701	6005	2096	461	3362	898	−240	−2643	−1198
4	VMAT	200 × 25	733	4536	2192	485	4196	1439	−249	−340	−753
5	VMAT	266 × 16	330	1891	733	289	1401	588	−41	−490	−145
6	VMAT	200 × 25	824	4937	2291	685	3939	1799	−139	−998	−492
7	VMAT	200 × 25	383	3287	1045	353	2894	926	−30	−393	−119
8	VMAT	200 × 25	450	3637	907	425	2900	811	−25	−737	−96
9	VMAT	200 × 25	528	5176	1157	496	4287	1137	−32	−889	−20
10	VMAT	200 × 25	431	3564	965	437	3647	1024	5	84	59
AVG			539	3954	1402	449	3188	1068	−90	−766	−335
STD			172	1276	601	107	952	339	95	731	411
P value									.02	.01	.03

Abbreviations: AVG = average; $D_{5\%}$ = 5% of the maximum dose; DIBH = deep inspiration breath hold; D_{Max} = maximum dose; D_{Mean} = mean dose; FB = free breathing; Rx = prescription; STD = standard deviation; VMAT = volumetric modulated arc therapy.

The heart dose reduction is significant ($P < .05$) with $\Delta D_{Max} = -7.7 \pm 7.3$ Gy, $\Delta D_{5\%} = -3.4 \pm 4.1$ Gy, and $\Delta D_{Mean} = -0.9 \pm 1.0$ Gy from FB to DIBH.

Table 3 Heart dose sparing based on tangent plan dosimetry comparison between free-breathing (FB) and deep inspiration breath hold (DIBH) for patients with left-sided breast cancer with abdominal-driven breathing and little vertical chest elevation ($\leq$5 mm)

	Planning		FB (heart, cGy)			DIBH (heart, cGy)			Heart sparing (cGy)		
Patient	Plan	Rx (cGy)	D_{Mean}	D_{Max}	$D_{5\%}$	D_{Mean}	D_{Max}	$D_{5\%}$	D_{Mean}	D_{Max}	$D_{5\%}$
11	2F	265 × 16	64	544	190	56	374	161	−8	−170	−29
12	2F	265 × 16	65	1425	234	62	1108	231	−2	−317	−3
13	2F	520 × 5	49	2251	176	51	574	187	3	−1677	12
14	2F	265 × 16	75	3189	232	73	1622	252	−2	−1567	20
15	2F	265 × 16	145	3969	434	92	1321	297	−53	−2648	−137
16	4F	200 × 25	411	4788	1940	209	2010	557	−202	−2778	−1383
17	2F	375 × 8	38	1677	119	42	2059	125	4	382	6
18	2F	265 × 16	100	3109	289	81	1535	239	−19	−1574	−50
19	2F	520 × 5	611	3720	1731	476	2638	886	−135	−1082	−845
20	2F	265 × 17	254	3165	699	253	3014	723	−1	−151	24
AVG	-	-	181	2784	604	139	1626	366	−42	−1158	−239
STD	-	-	191	1295	672	138	839	262	71	1082	481
P value	-	-	-	-	-	-	-	-	.10	.008	.15

Abbreviations: 2F = 2 fields (opposite tangent fields); 4F = 4 fields(opposite tangents, supraclavicular field, and posterior axillar boost field); AVG = average; $D_{5\%}$ = 5% of the maximum dose; DIBH = deep inspiration breath hold; D_{Mean} = mean dose; FB = free breathing; Rx = prescription; STD = standard deviation.

The heart-sparing $D_{Max} = -11.6 \pm 10.8$ Gy ($P = .008$) from FB to DIBH.

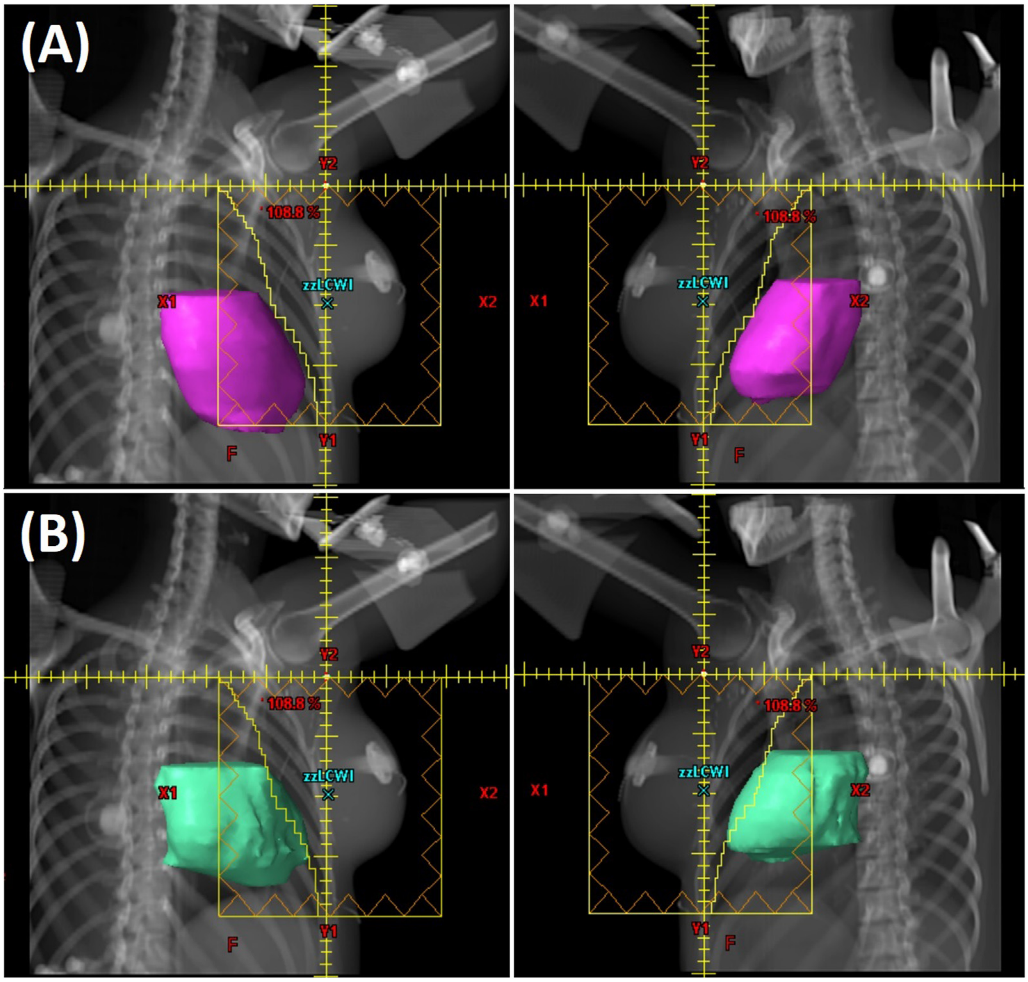

Figure 3 (A) Illustration of heart blocking (patient #11) in the DIBH tangent plan using multileaf collimators, which (B) may not block the heart in FB, resulting in the anterior-lateral portion of the heart inside the tangent fields and causing a much higher heart maximum dose, at or near the full prescribed dose. *Abbreviations:* DIBH = deep inspiration breath hold; FB = free breathing.

to higher heart doses even though VMAT plans are optimized to spare the heart as much as possible.[19] More importantly, the treatment target for the VMAT plan is usually larger, covering local lymph nodes, including the internal mammary node; therefore, this is also responsible for the higher heart dose. For these reasons, heart dose distribution in DIBH VMAT plans contains a large low-dose region and is very different from that of tangent plans. For instance, for D_{Mean} = 5 Gy, a tangent plan would need a considerable amount of the heart inside the beam field to raise the average between the full prescribed dose and near-zero background dose. For DIBH tangent plans, the heart is always blocked by the multileaf collimators (MLC), as shown in Fig. 3. However, the same MLC setting may not block the heart effectively in FB, leading to a much higher D_{Max} as the anterior-lateral portion of the heart may fall inside the opposite tangent fields.

Percentage of A-DIBH patients among the control group

The population of native abdominal-driven breathing patients is 6 of the 40 randomly selected control patients, about 15%, as shown in Table 4. Both the VCE (for SGRT ROI) and the motion of the surrogate (RPM/RGSC) are provided. Although the surrogate is placed around the xiphoid process, its motion represents a mix of both chest and abdominal motions due to its finite size (RPM: 3.4 cm and RGSC: 7.4 cm in the superior-inferior direction). Figure 4 shows the distributions of the chest ROI vertical motion based on the VCE values and surrogate motion data, suggesting the difference between surface-guided and surrogate-guided DIBH procedures. Within the FOV of FB and DIBH CT images, the most pronounced abdominal motion is also measured, indicating if the abdomen moves greater than the chest surface. Figure 5 provides a proposed

Table 4 Body surface elevations and surrogate motion at different locations among the 40 randomly selected patients with left-sided breast cancer DIBH in the control measurement

		Vertical chest elevation (mm)		Measured surrogate motion between FB and DIBH cts (mm)			Default gating threshold (mm)[*]		Abdomen motion[†] Greater?
Patient	Plan	Breast	Xiphoid	Type	Motion	Location	Lower	Upper	
21	T	16.6	13.0	RGSC	18.1	Chest	11.0	16.0	Y
22	T	8.5	10.1	RGSC	10.5	Chest	6.5	11.5	N
23[‡]	V	5.0	3.8	RPM	7.0	Chest	5.1	10.1	Y
24	T	12.6	12.0	RGSC	24.8	Chest	8.0	13.0	Y
25	V	13.1	13.0	RGSC	21.9	Chest	11.7	16.7	Y
26	T	16.1	16.6	RPM	25.3	Chest	27.6	32.6	M
27	V	13.2	11.5	RPM	8.5	Chest	13.2	18.2	Y
28	T	17.8	15.1	RPM	16.7	Chest	15.1	19.9	N
29[‡]	T	5.3	4.1	RGSC	25.6	Chest	26.9	31.9	N
30	T	11.8	15.5	RPM	25.9	Chest	27.1	32.1	N
31	T	10.4	8.2	RPM	13.9	Chest	12.6	17.6	Y
32	T	7.1	6.8	RGSC	16.5	Chest	8.0	13.0	Y
33	V	8.0	7.9	RPM	18.0	Chest	9.6	14.6	N
34[‡]	V	5.4	4.9	RPM	13.3	Chest	13.5	18.5	Y
35[‡]	V	4.8	4.9	RGSC	4.1	Chest	3.8	8.8	Y
36	T	10.5	5.7	RGSC	16.1	ABD	17.0	21.9	Y
37	V	6.8	10.0	RPM	24.5	Chest	18.5	22.5	M
38	T	16.8	17.3	RGSC	22.1	Chest	13.1	18.1	N
39	T	10.4	11.4	RPM	9.8	Chest	8.4	13.4	M
40	V	10.1	5.4	RGSC	9.3	Chest	8.7	13.7	N
41	V	19.9	15.3	RGSC	20.1	Chest	8.0	13.0	Y
42	V	18.4	15.2	RGSC	18.1	Chest	14.7	19.7	M
43	T	12.9	13.0	RPM	12.1	Chest	11.8	16.8	M
44	V	16.3	5.3	RGSC	10.4	ABD	8.0	13.0	Y
45	T	11.3	11.3	RGSC	28.2	Chest	20.0	25.0	Y
46	V	10.5	7.4	RGSC	18.6	Chest	11.8	16.8	M
47	T	11.3	10.8	RPM	10.4	Chest	15.6	20.6	Y
48	T	11.6	8.9	RGSC	9.5	Chest	9.7	14.7	M
49	T	12.2	10.6	RPM	10.3	Chest	7.3	12.3	N
50	T	21.1	20.2	RGSC	24.6	ABD	22.0	27.0	N
51[‡]	V	5.0	5.8	RPM	13.9	ABD	16.0	21.0	M
52	V	14.3	11.4	RGSC	8.3	Chest	6.1	11.1	Y
53	V	6.5	9.6	RPM	10.0	Chest	10.6	15.6	Y
54	V	9.6	6.3	RPM	5.8	Chest	8.0	13.0	M
55	V	6.0	6.8	RPM	7.3	Chest	6.2	11.2	Y
56	T	16.8	11.6	RGSC	20.6	Chest	16.0	21.0	M
57	T	6.0	6.9	RGSC	17.4	Chest	15.0	20.0	Y

(*continued on next page*)

Table 4 (*Continued*)

		Vertical chest elevation (mm)		Measured surrogate motion between FB and DIBH cts (mm)			Default gating threshold (mm)*		Abdomen motion[†]
Patient	Plan	Breast	Xiphoid	Type	Motion	Location	Lower	Upper	Greater?
58[‡]	T	4.0	6.0	RGSC	11.0	Chest	7.5	12.5	Y
59	V	14.4	15.8	RPM	21.3	Chest	20.1	25.1	Y
60	T	24.4	26.8	RGSC	25.6	Chest	25.5	30.5	N

Abbreviations: ABD = abdomen; DIBH = deep inspiration breath hold; FB = free breathing; Y = yes, M = maybe, N = no; T = tangents; V = volumetric modulated arc therapy, RGSC = respiratory gating for scanners with the box longitudinal length of 74 mm; RPM = real-time positioning management with the box longitudinal length of 34 mm .

* The default DIBH gating window is determined through the RPM or RGSC system.

† M is indicated for a larger abdominal motion due to insufficient ABD in the field of view of FB and DIBH computed tomography.

‡ Patients 23, 29, 34, 35, 51, and 58 have vertical chest elevation ≤5 mm.

Six patients are identified as abdominally-driven breathing individuals with little vertical chest elevation (≤5 mm).

clinical workflow to identify A-DIBH patients as early as simulation and apply a new abdomen ROI or switch to RPM/RGSC for A-DIBH monitoring.

Discussion

Identification of A-DIBH patients early in the clinical workflow

As abdominal-driven breathing patients account for about 15% (6 of 40) of the control group, a sizable portion of the patient population, these patients must be identified early in the clinical workflow, as shown in Fig. 5. This finding is consistent with a previous report of 27% A-DIBH in 22 patients studied,[16] suggesting that the population of A-DIBH patients is significant and must be treated accordingly. First, at simulation, it is the first opportunity to learn how a patient breathes into DIBH. After a brief patient training on how to perform DIBH near their maximum capacity without interference with the patient's native breathing behavior, therapists should check the vertical surface elevation at the xiphoid process and central abdomen before CT scans using a ruler and the horizontal room laser. Therefore, the abdominal-driven

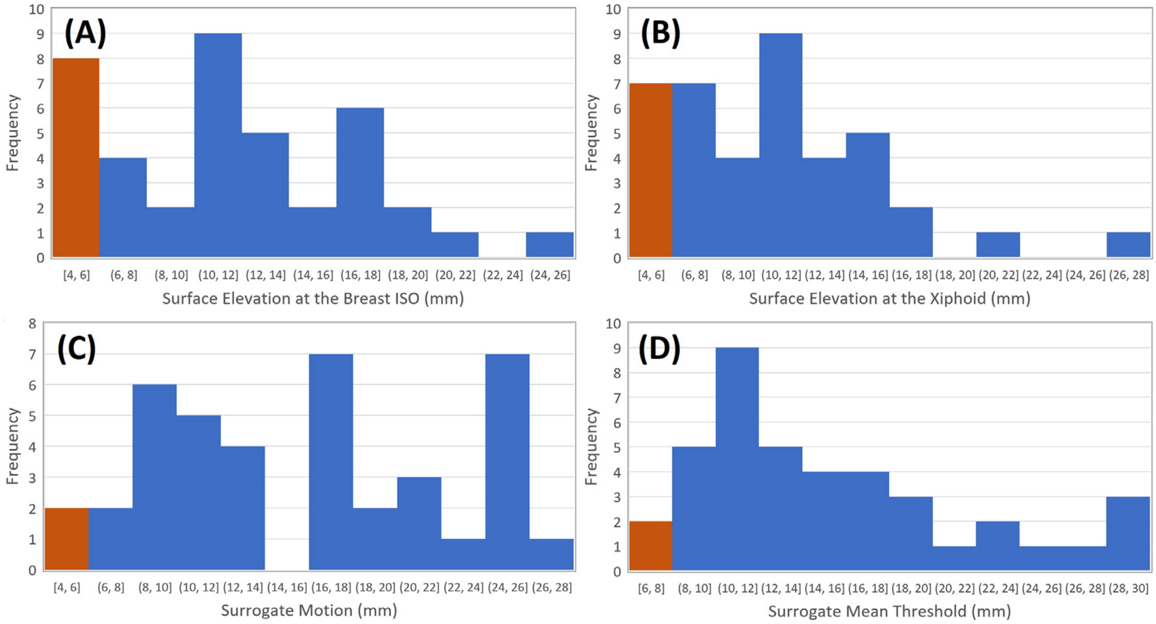

Figure 4 Histogram of chest surface elevation and surrogate motion and threshold in 40 control breast deep inspiration breath hold patients. The vertical elevation at (A) the breast ISO and (B) the xiphoid process has a significantly higher population of small values compared with (C) surrogate motion and (D) the default gating threshold. Even though the surrogate was placed around the xiphoid, it senses both thoracic and abdominal motion due to its finite size (RPM: 3.4 cm; RGSC: 7.4 cm in the superior-inferior direction). *Abbreviations:* ISO = isocenter, PRM = real-time positioning management, RGSC = respiratory gating for scanners.

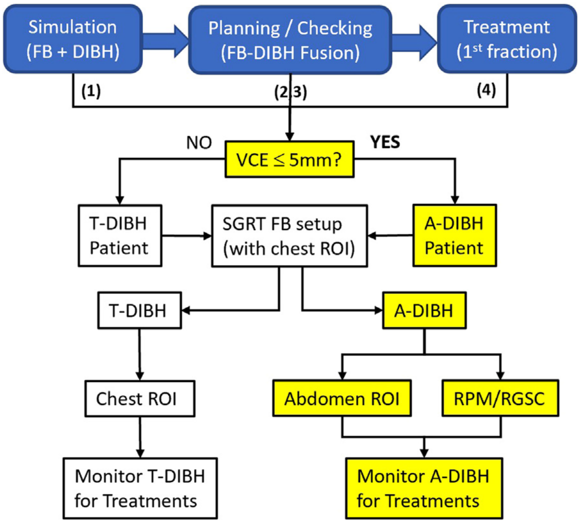

Figure 5 A proposed clinical workflow for online identification of A-DIBH patients and adaptation of an alternative ROI for surface-guided radiation therapy setup or use of RPM/RGSC as the backup method. Four opportunities to identify A-DIBH patients: (1) at simulation, (2) at planning and (3) plan checking, and (4) at the first treatment fraction. It is worthwhile to note that the chest-only ROI can be used for FB setup for both groups of patients: only from FB to DIBH does setup require a different motion monitoring technique. *Abbreviations:* A-DIBH = abdominal-driven DIBH; DIBH = deep inspiration breath hold; FB = free breathing; RGSC = respiratory gating for scanners; ROI = region of interest; RPM = real-time positioning management; T-DIBH = thoracic-driven DIBH; VCE = vertical chest wall elevation.

breathing patients can be identified before the CT scan, and the surrogate box should be placed interior to the xiphoid process with the maximum vertical motion. Furthermore, the information should be passed to the planning and treatment teams to use an appropriate motion monitoring technique for A-DIBH treatment.

Second, at the beginning of the planning process, the dosimetrist should check VCE when checking the alignment between the FB and DIBH CTs, and if VCE ≤ 5 mm, appropriate action should be taken, which is discussed in the next section. For tangent plans, a physician is often setting an MLC block to avoid the heart in the beam's eye view, and MLC motion is optimized to achieve a uniform dose in the midline of breast separation in the beam's eye view.[20,21] For VMAT planning, the heart is always set as the primary OAR (an avoidance structure) in plan optimization to achieve clinical goals. Because of a sharp dose falloff outside of the planned target volume in tangent fields or VMAT plan, a small heart-shape deformation (elongation) or position change (toward the inferior direction) due to the diaphragmatic pull at A-DIBH may lead to a significant reduction of D_{Max} (Tables 2 and 3, although D_{Mean} reduction (<1 Gy) may not be clinically significant.[1] The dosimetrist must assess if the surrogate position at the simulation is optimal to monitor the DIBH (motion >5 mm); otherwise, an inferior shift of the box may be warranted in the patient's setup instruction. Alternatively, the default chest-only ROI should be altered to include or shift to the central abdominal area till the inferior border within the CT FOV.

The third opportunity for identification of A-DIBH patients is at the second independent plan checking process in which a senior physicist checks plan quality and approves it for treatment delivery. The anterior VCE must be checked together with FB DIBH CT alignment. Similarly, the plan checker should work with the planner to change the patient setup instruction to provide appropriate instruction for DIBH monitoring. In fact, most of the A-DIBH patients were identified by the plan checkers in this study.

The last opportunity is at the first fraction of treatment, in which the therapists who conduct the DIBH SGRT treatment (default procedure) should check the ROI surface difference after FB setup using the DIBH reference. Whereas in FB, the real-time motion monitoring will show the shift of the FB from DIBH; if a little vertical shift (VCE ≤ 5 mm) is identified using the default chest-only ROI, the therapists should inform the planner and plan checker to resolve this clinical issue first before treatment. The action tolerance threshold of 3 mm is usually kept unchanged unless a patient had difficulties reproducing the depth of DIBH after several trials. Also, a near-miss event should be reported via the institutional reviewing board for assessment by a dedicated clinical safety reading group.

Clinical solutions for proper monitoring of A-DIBH patients

The surrogate-guided and surface-guided motion monitoring indicators of DIBH are not equivalent, as they monitor different parts of the anterior surface and, thus, sense different motions. Therefore, their differences must be characterized thoroughly to avoid any potential pitfalls in routine clinical operations. As shown in Fig. 4, although the xiphoid process is included in both motion monitoring techniques, different results may occur, especially for A-DIBH patients. In the 40 control patients in this study, RPM/RGSC is still effective (motion >5 mm) in 95% of cases to monitor DIBH, including the abdominal-driven breathing patients, as it covers part of the upper abdominal surface due to its finite length (RPM: 3.4 cm and RGSC: 7.4 cm). However, the SGRT approach with a chest-only ROI (Fig. 1) is not suitable for A-DIBH as the ROI does not sense the abdominal motion. Therefore, caution must be paid when adopting the SGRT technology for left-sided breast DIBH treatment so that most breathing behaviors are covered.

Here, 2 feasible clinical solutions are suggested to cover abdominal-breathing patients without substantial changes to the existing clinical practice. First, within the SGRT approach, the ROI should be altered to cover the central part of the abdominal surface, which is correlated ($r > 0.6$) with the diaphragm motion.[22] The soft abdominal surface is not supported by the rib cage, which is moving with the chest. To ensure significant motion detection in SGRT for abdominal-driven breathing patients, a second ROI could be created on the central abdominal surface to sense the abdominal surface motion, distinguishing A-DIBH from FB, whereas the default chest-only ROI can still be used for FB setup (Fig. 5). In fact, a recent study on automatic ROI definition using deep learning reported that the learned ROI includes the abdominal surface in 5 of 10 tested patients.[23] Second, it is an option to switch the motion monitoring technique from SGRT to RPM/RGSC, as the DIBH scan at simulation is guided by the surrogate in our institution and used as the backup method in case the AlignRT system is down. However, the surrogate position may need to be shifted inferiorly, as shown in Fig. 1 and Table 1, in which 8 of 20 patients (40%) have a small surrogate motion (4 ± 1 mm) but higher abdominal motion (11 ± 2 mm) inferior to the clinical surrogate position. It is worthwhile to note that studies have shown similar setup accuracy between surface-guided and surrogate-guided procedures, whereas SGRT has the advantage of timesaving in the process.[5,24] Clinically, as long as A-DIBH patients are identified before treatment (Fig. 5), the abdominal-driven breathing patients will be treated correctly with expected heart sparing, as shown in Tables 2 and 3.

Alternatively, but with a substantial change in the current clinical practice, a more intensive patient training and visual coaching program could be introduced to uniformly train all patients to go through chest-driven breathing and ensure T-DIBH throughout the treatment. This means that the native breathing behavior of A-DIBH patients must be consistently altered, which was previously reported.[6,14] However, it is necessary to conduct daily visual feedback guidance, perhaps reinforced training, to allow patients to follow the trained breathing behavior throughout the multifractional treatment, so patients would not fall back to their native breathing behavior. In our clinics, patients are only instructed with a few brief DIBH practices with no intention to change their native behavior before CT scans at simulation, similar to another report,[9] and guided to perform daily DIBH with audio feedback during SGRT treatment. The purpose of the initial training is to allow patients to get used to the DIBH process and reach their maximal capacity. Since patients' native breathing behavior is not altered, the DIBH treatment tends to be more consistent and reproducible.

Heart sparing for abdominal-driven breathing patients in SGRT DIBH treatment

Recently, 3 comparison studies on the benefit of heart sparing by training patients to perform T-DIBH and A-DIBH versus FB at CT simulation used 2 planning methods: 3-dimensional conformal radiation therapy and intensity modulated radiation therapy.[16-18] Our results in dosimetry and population of A-DIBH patients are consistent with theirs, showing heart sparing benefit of A-DIBH. By comparing the dosimetry of the plans, both Zhao et al[16] and Matsumoto et al[18] concluded that significantly lower doses to the heart in A-DIBH than in T-DIBH, although Hirata et al[17] found similar heart doses in both DIBHs, much lower than FB, confirming the benefit in heart sparing for abdominal-driven breathing patients with breast cancer.

Zhao et al[16] reported 27% native A-DIBH patients (6 of 22), which is consistent with our finding of 15% (6 of 40), suggesting a significant patient population that must be treated differently. However, our approach to handling A-DIBH clinically is fundamentally different from theirs, as we believe the patient's native breathing behavior is more reproducible and should not be altered. In fact, Matsumoto et al[18] reported that among 120 patients, 20 could not follow the training to properly perform T-DIBH or A-DIBH in CT simulation, so they were excluded from that study, and only 100-patient results were reported.[18] In reality, such events could occur in the clinic at simulation and/or treatment, resulting in these patients' exclusion from DIBH treatment; otherwise, such uncertainty has to be accepted for DIBH treatment. Although A-DIBH may lower the heart dose more than T-DIBH, the number of A-DIBH patients is significantly smaller than T-DIBH, so changing most patients' breathing behavior (73%-85%) could introduce substantial uncertainty, which could diminish the slight benefit of heart sparing in A-DIBH. After all, the previous reports support our clinical approach that patients' native behavior should be preserved for higher DIBH reproducibility, and training and coaching patients to go through an unfamiliar DIBH process may pose a substantial challenge, as 17% of patients (20 of 120) could not follow the guidance[18] and the tendency of falling back to patients' natural breathing behavior.

In our radiation therapy clinics, DIBH breast treatment is decided by an attending physician at simulation if DIBH can help to achieve extra heart-chest wall separation compared with FB based on CT simulation. For patients with early stage disease, both tangent DIBH and prone treatment planning are viable options, whereas for patients with late-stage disease, VMAT or tangents with supraclavicular field and posterior axillary boost field at DIBH are often used. In tangents planning, a heart MLC block is usually drawn by the attending physician to achieve heart sparing (Fig. 3), whereas in VMAT planning, the heart is set as the primary OAR to spare.

For the 20 A-DIBH patients, the dosimetric comparison of FB and DIBH plans using the same technique shows that the most significant OAR sparing is the heart dose reduction in D_{Max} and $D_{5\%}$ ($P < .05$). Although the <1 Gy reduction of D_{Mean} is also statistically significant, clinically it may not be significant as the risk of long-term heart ischemic event is reduced by only <20% with a D_{Mean} reduction of <1 Gy.[1] For tangent plans, the heart $\Delta D_{Mean} = -1.4 \pm 1.4$ Gy is already low at DIBH (Table 3) by using the MLC heart blocking. The most significant heart dose reduction is $\Delta D_{Max} = -11.6 \pm 10.8$ Gy ($P = .01$), which reflects high-dose volume reduction of the heart away from the tangential beams. Therefore, the left anterior descending (LAD) coronary artery and left ventricle (LV) can be effectively spared from FB to DIBH.[25,26] In a 2013 report on the risk of ischemic heart disease from radiation therapy by Derby et al,[1] the increase of the D_{Mean} in tangent treatment is directly related to the high-dose heart volume, which may include the LAD and LV.

VMAT planning tends to produce a higher D_{Mean} (4.5 ± 1.1 Gy) at DIBH due to beam exits and internal mammary node coverage, but heart toxicity is manageable.[19,27] The 1-Gy heart mean dose reduction may only result in a 7.4% reduction of heart ischemic events, according to the 2013 report.[1] However, the report based on patients with left-sided breast cancer treated with tangent plans may not apply to the VMAT plan, as it has a very different dose distribution from a tangent plan. For instance, the heart D_{Max} in tangent treatment at FB is almost constant near the full prescribed dose if a part of the heart is inside the beam fields; therefore, only the D_{Mean}, a volume-weighted average dose between the full dose and negligible background dose in a tangent plan, may have a linear relationship with the heart ischemic events. In VMAT planning, the local lymph nodes, including the internal mammary node, are also the targets, and multiple beams are used that may exit from the heart, leading to an inevitably higher low-dose volume, even though the inverse planning tries to minimize the heart dose (as the primary OAR) through optimization. Therefore, although the D_{Mean} is higher in the VMAT DIBH plan, and the volume that receives the full prescribed dose is small, the heart ischemic event is clinically manageable,[6,14] different from the report.[1]

From FB to DIBH, because of the elongated heart shape and inferiorly shifted heart position, the anterior surface of the heart moves more inferiorly and/or medially by a few mm or even a few cm (Fig. 2); therefore, the increased separation effectively reduces the heart D_{Max} by 7.7 ± 7.3 Gy ($P < .05$) and $D_{5\%}$ by 3.4 ± 4.1 Gy. In our clinics, LAD and LV are not routinely contoured as avoidance structures so they cannot be evaluated quantitatively. However, as the LAD and LV are located on the anterior and lateral side of the heart and, thus, tend to receive the highest radiation dose, the D_{Max} reduction often correlates with dose reduction to the LAD and LV. Therefore, DIBH is still an effective approach to treating abdominal-driven breathing patients with left-sided breast cancer with a significant heart-sparing benefit, even when a small VCE ≤ 5 mm is observed.

Last, it should be noted that the dosimetric study reported here presents the worst-case scenario as the patient is unlikely to be in full FB status throughout the entire treatment session despite ineffective SGRT monitoring due to small VCE, which cannot distinguish FB from A-DIBH. Therefore, more realistic setups would be random distribution over the course of multifractional treatment, and the dosimetric effect would likely be smaller than depicted in this work. The dosimetric comparison aimed to show that (1) A-DIBH can spare the heart, and (2) it is important to identify A-DIBH patients so they can be treated optimally with proper heart sparing. Our results are consistent with the previous studies,[16-18] demonstrating the lowered heart dose by A-DIBH compared with FB. In the future, we plan to investigate actual heart doses between T-DIBH and A-DIBH patients using daily 2DkV data that are prescribed and acquired for VMAT patients with locally advanced disease.

Conclusion

A significant amount of DIBH patients (15%) with left-sided breast cancer in the control group of this study are native abdominal-driven breathing patients with little VCE (≤5 mm) from FB to A-DIBH. Clinically, abdominal-driven breathing patients can be benefitted from DIBH treatment, but they must be identified early in the clinical SGRT workflow during simulation, planning, plan checking, or at the latest the first fraction treatment so that appropriate motion monitoring techniques can be applied to ensure reproducible A-DIBH for heart-sparing. Immediate clinical solutions should be either to create a second ROI to include the central abdominal surface for DIBH setup in SGRT or to switch the motion monitoring technique to RPM/RSGC with a possible inferior placement shift when applicable. With these suggested solutions, patients with left-sided breast cancer with native abdominal-driven breathing behavior can still benefit from DIBH treatment with heart sparing.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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